

MAR 22 2001

Sigma Diagnostics, Inc.
ThromboMAX™ HS with Calcium

Summary of Safety and Effectiveness

Sigma Diagnostics ThromboMAX™ HS with Calcium is a lyophilized preparation of thromboplastin derived from rabbit brain with buffers, stabilizers, and calcium ions. It is intended for use in the one-stage Prothrombin Time (PT) test and in PT based assays.

Thromboplastin is an extractable complex from many mammalian tissues which, in combination with calcium ions, accelerates the clotting of blood by activation of the extrinsic pathway of coagulation.^{1,2,3} This property lead to the development of a simple, rapid diagnostic assay now widely known as the Prothrombin Time (PT) test.^{4,5,6} The PT test is widely used as a pre-surgical screen for bleeding disorders and for monitoring anti-coagulant therapy.^{7,8} Dicumarol and related drugs reduce the activity of the vitamin K-dependent clotting factors II, VII, IX, X, Protein C, and Protein S^{9,10} and thereby prolong the PT. The PT assay is also used in the quantitative determination (Factor Assays) of Factors II, V, VII, and X.

The safety and effectiveness of Sigma Diagnostics ThromboMAX™ HS with Calcium (product numbers T9561 and T9686, herein referred to as "ThromboMAX HS") has been demonstrated by showing it's substantial equivalence to Sigma Thromboplastin HS with Calcium (product numbers T4552 and T6540, herein referred to as "Thromboplastin HS").

Fifty random patient samples were assayed on the Amelung 190 Plus in both optical and mechanical modes with the described ThromboMAX HS reagent (y) and with the Thromboplastin HS reagent (x). Comparison of the results yielded correlation coefficients and regression equations of 0.974 and $y=1.154*x - 0.911$ for the optical method, and 0.977 and $y=1.15*x - 1.033$ for the mechanical method.

Imprecision studies demonstrated the following within-run (S_{wr}) and total imprecision (S_t) coefficients of variation:

<u>Control Plasma</u>	CS-190 Optical		CS-190 Mechanical	
	$S_{wr}CV$	S_tCV	$S_{wr}CV$	S_tCV
Level I	0.48%	0.76%	0.85%	1.44%
Level II	0.62%	1.94%	0.87%	1.82%

References:

1. Quick, A.J., "On Various Properties of Thromboplastin (Aqueous Tissue Extracts), *Am. J. Physiology* 1936, 114: 282.
2. Nemerson, Y., "Characteristics and lipid requirements of coagulant proteins extracted from lung and brain; the specificity of the protein component of tissue factor", *J. Clin. Pathology* 1969, 48: 322.
3. Davie, E.W., Fujikawa, K., and Kisiel, W., "The Coagulation Cascade: Initiation, Maintenance, and Regulation", *Biochemistry* 1991, 30: 10363.
4. Quick, A.J., "The Prothrombin in Hemophilia and in Obstructive Jaundice", *J. Biol. Chemistry* 1935, 109: 73.
5. Quick, A.J., "The Nature of the Bleeding in Jaundice", *J. Am. Med. Assoc.* 1938, 110: 1658.
6. Quick, A.J., "Thromboplastin as a Reagent", *Thromb. Diath. Haemorrhage* 1970, 23: 585.

7. Errichetti, A.M., Holden, A., Ansell, J., "Management of Oral Anticoagulant Therapy: Experience with an Anticoagulation Clinic", *Arch. Inter. Medicine* 1984, 144: 1966.
8. Hirsh, J., Dalen, J.E., Deykin, D., Poller, L., "Oral Anticoagulants: Mechanisms of Action, Clinical Effectiveness, and Optimal Therapeutic Range", *Chest* 1992, 102 (suppl): 312S.
9. Miale, J.B., "Laboratory Medicine - Hematology, 4th edition", C.V. Mosby, St. Louis, 1972.
10. Furie, B., and Furie, B.C., "Molecular and Cellular Biology of Blood Coagulation", *N. Eng. J. Medicine* 1992, 326: 800.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

William R. Gilbert, Ph.D.
Manager, Scientific Affairs
Sigma Diagnostics, Inc.
545 South Ewing Avenue
St. Louis, Missouri 63103

Re: K010158
Trade Name: Sigma Diagnostics ThromboMAX™ HS with Calcium
Regulatory Class: II
Product Code: GGO
Dated: January 15, 2001
Received: January 17, 2001

Dear Dr. Gilbert:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895.

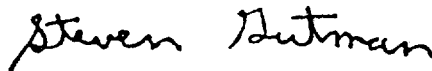
A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

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This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsma/dsmamain.html>".

Sincerely yours,

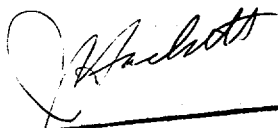
A handwritten signature in black ink that reads "Steven Gutman". The signature is written in a cursive, slightly slanted style.

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known): K010158Device Name: Sigma Diagnostics ThromboMAX™ HS with Calcium**Indications For Use:**

Sigma Diagnostics ThromboMAX™ HS with Calcium is a device used as a general screening procedure for the detection of possible clotting factor deficiencies in the extrinsic coagulation pathway which involves the reaction between coagulation factors III and VII, and to monitor patients receiving coumarin therapy (the administration of one of the coumarin anticoagulants in the treatment of venous thrombosis or pulmonary embolism).


(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K010158

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ☒
(Per 21 CFR 801.109)

OR

Over-The-Counter Use ☐